

Tularemia

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To assist in diagnosis.
2. When the source is a risk for only a few individuals (e.g., animal exposure), to inform those individuals how they can reduce their risk of exposure.
3. To educate potentially exposed persons, including laboratory personnel, about signs and symptoms of disease, thereby facilitating early diagnosis.
4. To determine the endemicity and epidemiology of the disease in Washington state.
5. To raise the index of suspicion of a possible bioterrorism event if no natural exposure source is identified.

B. Legal Reporting Requirements

1. Health care providers: notifiable to local health jurisdiction within 3 work days.
2. Hospitals: notifiable to local health jurisdiction within 3 work days.
3. Laboratories: notifiable to the local health jurisdiction within 2 work days; specimen submission required.
4. Veterinarians: notifiable to Washington State Department of Agriculture or to the local health jurisdiction.
5. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. **If bioterrorism is suspected, immediately report the case to DOH: 1-877-539-4344.**
2. Facilitate the transport of specimens to DOH Public Health Laboratories (PHL) for confirmatory testing.
3. Educate potentially exposed persons, including laboratory personnel, about signs and symptoms of disease and recommend antibiotic prophylaxis if indicated.
4. Report all *confirmed* and *probable* cases to CDES (see definitions below).
Complete the tularemia report form
(<http://www.doh.wa.gov/notify/forms/tularemia.doc>) and enter the data in the Public Health Issues Management System (PHIMS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Francisella tularensis are small, aerobic, non-motile, gram-negative coccobacilli. Two subspecies causing most human disease are *F. tularensis* subsp. *tularensis* (Jellison type A) and *F. tularensis* subsp. *holarctica* (Jellison type B). Type A tends to cause more severe disease than type B.

B. Description of Illness

The nature of the illness usually reflects the route of transmission, as well as the virulence of the infecting strain. Almost all cases have a rapid onset of fever, chills, malaise and headache along with symptoms falling into one or more of the following categories:

1. Ulceroglandular

Patients present with a papule that develops into a non-healing skin ulcer at the inoculation site (i.e., insect or animal bite) and large, tender lymph nodes.

2. Glandular

Patients present with large, tender lymph nodes without skin lesions.

3. Oculoglandular

Patients present with severe, painful conjunctivitis (usually unilateral) with regional lymphadenopathy.

4. Oropharyngeal

Patients present with severe throat pain with exudates on the throat and tonsils and cervical adenopathy after ingestion of contaminated food, water, or droplets.

5. Pneumonic (pulmonary)

Pneumonic tularemia occurs as a primary infection following inhalation of organisms, or may be secondary to bacteremia/septicemia as blood-borne organisms localize in the lung or pleural spaces. The pneumonic form is the most probable presentation of illness in a bioterrorist attack. It resembles plague, with symptoms including fever, non-productive cough, and pleuritic chest pain. Patchy bilateral infiltrates, pleural effusion and hilar adenopathy may be seen on chest X-ray.

6. Septicemic or Typhoidal

Septicemic tularemia can develop after any mode of acquisition. Patients may present with a variety of symptoms including fever, chills, headache, muscle aches, sore throat, abdominal pain, diarrhea, and vomiting. This form of blood-borne infection can also lead to shock, DIC or other complications.

C. Tularemia in Washington State

Tularemia is an endemic zoonosis in Washington where 1 to 10 tularemia

infections are reported annually. Potential sources of infection reported by Washington residents with tularemia include insect and animal bites, contaminated water, and aerosol exposure while farming or using power landscape tools such as lawn mowers and weed eaters. Epidemiological data from human cases with endemic exposures indicates that tularemia is most commonly acquired in western Washington. The majority of *F. tularensis* isolates in Washington are type B.

A statewide serosurvey of more than 360 outdoor pet cats and dogs in Washington during 2004–2005 indicated that 0.6% were exposed to tularemia. The incidence was highest in dogs and cats tested in southwest Washington (4.5%).

D. Vectors and Reservoirs

The primary reservoirs of *F. tularensis* include wild mammals (especially rabbits, hares, voles, squirrels, muskrats, beavers). Arthropods that bite these animals (e.g., ticks, deerflies) act as vectors to help maintain the life cycle of the organism and can themselves remain infective for prolonged periods. Humans and domestic animals are usually dead-end hosts (i.e., they do not transmit the infection to others).

E. Modes of Transmission

Infection can occur by direct contact with an infected animal, arthropod bite, ingestion of contaminated meat or water, or inhalation of the organism. As noted above, the infection progresses from the portal of entry, thereby determining the form of illness.

In Washington approximately 50% of cases may be transmitted by aerosolization of contaminated dust while using farm and landscaping equipment. This exposure causes the pneumonic form of tularemia. Common sources of ulceroglandular tularemia include arthropod bites (ticks, deer flies); animal bites; and inoculation of skin with contaminated water, blood or tissue (e.g., handling animal carcasses). Inoculation of eyes with contaminated stream water has occurred in Washington. Infection after eating undercooked meat of infected animals or drinking contaminated water is uncommon in humans regionally, but is effective in transmission among animals.

This organism is extremely dangerous to handle in the medical laboratory; culture of material from patients with suspected tularemia should not be attempted without special containment facilities. Contact PHL for additional information.

F. Incubation Period

Ranges from 1–14 days, but usually 3–5 days.

G. Period of Communicability

Not directly transmitted from person to person. Unless treated, the infectious

agent may be found in the blood during the first two weeks of disease and in lesions for a month, sometimes longer.

F. tularensis is quite hardy, surviving in water, mud, and animal carcasses for prolonged periods. Rabbit meat frozen at -15°C (5°F) has remained infective longer than 3 years.

H. Treatment

Tularemia is treated with appropriate antibiotic therapy. For further details regarding treatment see:

<http://www.bt.cdc.gov/agent/tularemia/index.asp#treatment>.

3. CASE DEFINITIONS

A. Clinical Criteria for Diagnosis

An illness characterized by several distinct forms, including the following:

- Ulceroglandular (cutaneous ulcer with regional lymphadenopathy)
- Glandular (regional lymphadenopathy with no ulcer)
- Oculoglandular (conjunctivitis with preauricular lymphadenopathy)
- Oropharyngeal (stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy)
- Intestinal (intestinal pain, vomiting, and diarrhea)
- Pneumonic (primary pleuropulmonary disease)
- Typhoidal (febrile illness without early localizing signs and symptoms).

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *F. tularensis*, exposure to potentially contaminated dust or water, or laboratory exposure.

B. Laboratory Criteria for Diagnosis

1. Presumptive:

- Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination, or
- Detection of *F. tularensis* in a clinical specimen by fluorescent assay.

2. Confirmatory:

- Isolation of *F. tularensis* in a clinical specimen, or
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen.

C. Case Definition (1999)

1. Probable: a clinically compatible case with presumptive laboratory results.
2. Confirmed: a clinically compatible case with confirmatory laboratory results.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Diagnosis

F. tularensis can be isolated from a variety of bodily fluids and tissues including wound exudate, lymph node, pleural fluid, and blood, but isolation requires processing on special culture media. It is a highly infectious organism, and is known to cause infection in laboratory workers. Laboratory personnel should be alerted if tularemia is suspected. Suspect cultures should be immediately sent to a reference laboratory with BSL3 capabilities. Intense caution should be used to avoid exposure within the laboratory by aerosol. **Confirmatory laboratory testing must be performed by a reference laboratory such as the Washington State Public Health Laboratories (PHL).**

Recently, rapid diagnostic tests have been developed since *F. tularensis* is under surveillance as a potential agent for bioterrorism. Rapid laboratory tests include direct fluorescent antibody testing, time resolved fluorescence, and polymerase chain reaction.

The diagnosis of tularemia can also be made by acute and convalescent serological studies. A single convalescent specimen can be tested, but results may be inconclusive.

B. Tests Available at the Washington State Public Health Laboratories (PHL)

PHL can culture clinical specimens for *F. tularensis* and can provide identification of *F. tularensis* from pure isolates. PHL can also determine the biotype of the isolate using biochemical tests. Serologic tests are not performed at PHL but will be forwarded to the CDC for testing (biotyping is not possible from serology). PHL also performs rapid diagnostic testing in suspected bioterrorism situations. Contact CDES for approval prior to collection and shipment of specimens.

C. Specimen collection

1. Serologic tests

For antibody testing, 1–2 ml of both acute and convalescent sera are preferred. Submit serum in tightly sealed screw-cap tube with Parafilm M™ or pressure-sensitive labeling tape. Place labeled tubes in individual self-sealing plastic bags. Use sufficient absorbent material to secure contents and contain any leakage during shipment. Ship cold, not frozen with the PHL serology form (<http://www.doh.wa.gov/EHSPHL/PHL/Forms/Serology.pdf>).

2. *F. tularensis* isolates

Clinical laboratories need to call PHL prior to shipping isolates (206-418-5400). Isolates should be submitted with a completed PHL Reference Bacteriology Examinations form (<http://www.doh.wa.gov/EHSPHL/PHL/Forms/ReferenceBacteriology.pdf>).

5. ROUTINE CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent information. (For evaluation of a possible bioterrorist event, see Section 7 – Managing Special Situations)

A. Evaluate the Diagnosis

Collect copies of laboratory results. **Confirmatory laboratory testing should be performed by a reference laboratory such as PHL.** Facilitate submission of laboratory specimens to PHL for confirmation. Proceed with investigation after presumptive or confirmatory laboratory results are available for sporadic cases. During an outbreak event or a potential bioterrorism situation, start investigation before laboratory results are available if needed.

B. Identify Potential Sources of Infection

Review clinical presentation and history to determine appropriate potential exposures (i.e., pneumonia would indicate most likely inhalation exposure [use of landscaping or farming tools, dust, bioterrorism]; ulceroglandular tularemia would indicate possible inoculation via insect or animal bite/handling). Investigate possible exposures during the period 1–14 days before onset, including a history of:

1. Skinning or eviscerating wild game (especially rabbits or wild rodents);
2. Bites or scratches by wild or domestic animals;
3. Increased biting fly activity in the area and/or fly bites (deer and horse flies are usually active between late spring and early fall);
4. Recent tick bite;
5. Drinking untreated water or exposure to untreated water;
6. Eating inadequately cooked wild game (especially rabbit);
7. Contact or possible contact with dust or other aerosols associated with soil, grain or hay;
8. Work in a laboratory.

C. Identify Potentially Exposed Persons

1. Identify persons who participated with the case in any of the activities listed above and contact them, as well as any acquaintance or household member with similar illness. (Note: Anyone meeting the probable case definition should be reported and investigated in the same manner as a confirmed case.) If any are ill, inform them (or their physician) of possible exposure, in order to facilitate proper diagnosis and therapy.
2. Identify laboratory workers and health care providers exposed to specimens or laboratory isolates and educate them of symptoms of illness to facilitate diagnosis. See Management of Other Exposed Persons below for prophylactic

antibiotic recommendations.

6. CONTROLLING FURTHER SPREAD

A. Infection Control Recommendations

Hospitalized patients should be cared for using standard precautions.

B. Case Management: No follow-up is needed.

C. Contact Management: None since the infection is not spread person-to-person

D. Management of Other Exposed Persons¹⁻³

1. For persons with *high-risk* exposures, recommend doxycycline or ciprofloxacin orally for 14 days.
2. For persons with *low-risk* exposures or persons previously vaccinated, recommend observation for fever and other signs of illness without antibiotics.

¹ Penn RL. *Francisella tularensis* (Tularemia). In: Mandell GL, Bennett JE, Dolin R, eds. Mandell, Douglas, and Bennett's Principles of Practice of Infectious Diseases Sixth Edition. Philadelphia: Elsevier Churchill Livingstone; 2005:2674–85.

² Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: Medical and public health management. JAMA 2001;285:2763–73.

³ Centers for Disease Control and Prevention. Outbreak of Tularemia Among Commercially Distributed Prairie Dogs, 2002. MMWR 2002;51(31):688,699.

E. Environmental Measures

1. If the source of infection appears to be associated with rabbit or rodent hunting this fact should be publicized, in order to encourage proper handling of wild game carcasses. CDES and the Washington Department of Fish and Wildlife should be given prior notice of any media releases on game-associated tularemia.
2. If the suspected source is farm animals, contact CDES which will contact the Washington State Department of Agriculture.
3. If waterborne transmission is suspected from a drinking water source, the water supply will need to be decontaminated. Contact CDES which will contact the DOH Office of Drinking Water.

7. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

F. tularensis has been classified as a "category A" agent (of greatest concern) for bioterrorism because of its very low infectious dose (10–50 organisms), its ability to survive in the environment, the fact that it can be easily disseminated by aerosol, and that untreated inhalational tularemia has the capacity to cause severe illness and death. One should suspect bioterrorist spread of tularemia if there is a cluster of unusual pneumonia (atypical patient profile, e.g., young, otherwise healthy individuals, severe illness, low response to standard treatment)

particularly in persons in a building with a common ventilation system. ***Call CDES immediately (24/7) at 1-877-539-4344.***

In the setting of a biological attack, antibiotic prophylaxis with ciprofloxacin or doxycycline may be recommended for those with a suspected or known exposure to *F. tularensis*, as determined by public health officials, for 14 days post-exposure.

8. ROUTINE PREVENTION

A. Immunization recommendations

There is currently no licensed vaccine available against tularemia.

B. Prevention recommendations

1. Hunters, trappers, and food preparers should be instructed to wear gloves when skinning wild game and to keep their hands / gloves away from their eyes. They should thoroughly wash their hands after handling wild game carcasses. Wild game meat should be cooked "well done" (to at least 74°C/165°F).
2. Persons should be instructed to drink only treated water when in wilderness areas to avoid bacterial and protozoan diseases that can be transmitted via surface water.
3. Persons should avoid tick and insect bites when in high-risk areas.
 - Wear long pants and a long-sleeved shirt. Tuck your pant legs into socks or boots and shirt into pants. This can help keep ticks on the outside of your clothing where they can be more easily spotted and removed.
 - Wear light colored, tightly woven clothing which will allow the dark tick to be seen more easily. The tight weave makes it harder for the tick to attach itself.
 - Use tick repellent when necessary, and carefully follow instructions on the label. Products containing DEET or permethrin are very effective in repelling ticks. Take special care when using repellents on children.
 - Check yourself, your children and pets thoroughly for ticks. Carefully inspect areas around the head, neck and ears. If you find a tick attached to your skin, promptly remove it. Grasp the tick using tweezers as close to the skin as possible. With a steady motion, pull the tick straight out. Wash your hands and apply antiseptic to the bite. Do not crush ticks *in situ*; this could result in direct inoculation of spirochetes. For more information about removing a tick, visit: http://www.cdc.gov/ncidod/dvbid/lyme/ld_tickremoval.htm
 - Monitor the bite and be alert for early symptoms of tick-borne disease particularly "flu-like" symptoms or rash over the next month or so. If you develop symptoms, contact your health care provider.

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UPDATES